REMARKS

I. Status of the Claims

Claims 4-7, 12-49 are withdrawn from consideration as being drawn to a non-elected invention. Claim 11 is canceled. Claims 1 as amended, claims 2-3, and 8-10 are currently under examination on their merits. Support for the amendments can be found, for example, on pages 91 and 92 of the application as originally filed. Applicants submit that the current amendments contain no new matter.

II. Priority

Applicants acknowledge the Examiner's priority determination.

III. Claim Rejections Under 35 U.S.C. §112 Second Paragraph

The Examiner rejected claims 1-3 and 8-11 for allegedly being incomplete for omitting essential steps. Applicants have amended claim 1 to include the phrase "by contacting the cell with a p19ARF protein fragment, wherein the p19ARF protein fragment has the amino acid sequence as set forth in SEQ ID NO:10." Applicants respectfully submit that the amendment has overcome the rejection.

IV. Claim Rejections Under 35 U.S.C. §102(b)

Claims 1-3, 8, and 11 are rejected under 35 U.S.C. §102(b) in view of U.S. Patent No. 5,723,313 by Sherr et al. (hereinafter "Sherr et al."). Specifically, the Action asserts that Sherr et al. disclosed a method of using ARF-p19 to inhibit growth of cancer cells without understanding the mechanism. The Action takes the position that because it was recently discovered that p19ARF protein inhibits tumor cell proliferation by interacting with FoxM1B and preventing FoxM1B from entering nucleus, Sherr et al. inherently anticipate the subject matter of claims 1-3, 8, and 11.

Applicants have amended claim 1 to recite a p19ARF protein fragment, wherein the protein fragment has the amino acid sequence as set forth in SEQ ID NO: 10, which contains

amino acid residues 26 to 44 of p19ARF. Claim 11 is now canceled. Sherr et al. do not teach a method of inhibiting tumor cell proliferation by contacting cells with a p19ARF protein fragment having the sequence of SEQ ID NO: 10. Thus, Sherr et al. do not explicitly teach the current invention.

Additionally, Sherr et al. does not inherently anticipate the current invention. "In relying upon the theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art" (M.P.E.P. §2112 IV (quoting *Ex parte Levy*, 17 U.S.P.Q. 2d 1461, 1464) (emphasis original)). The Action has failed to provide such a basis. Contrary to the Action's assertion, Sherr et al. never demonstrated the use of any p19ARF fragment, instead of the full length protein, to inhibit tumor cell proliferation. Sherr et al. do not teach or suggest the ability of a protein fragment having amino acid residues 26-44 of p19ARF in inhibiting tumor cell proliferation. One of ordinary skill in the art would not have reasoned or envisaged the use of a protein fragment having the sequence as set forth in SEQ ID NO: 10, instead of the full length protein, to treat cancer cells in view of Sherr et al. The subject matter of current invention does not "necessarily flow from" the teachings of Sherr et al. Thus, the cited art neither explicitly nor inherently anticipates claims 1-3 and 8-10. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(b).

V. Claim Rejections Under 35 U.S.C. §103(a)

Claims 1 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. in view of Laes et al. Specifically, the Action asserts that it would have been obvious to one skilled in the art to use p19ARF to treat hepatocellular carcinoma in view of the combination of the cited art. Applicants respectfully traverse the rejection.

The Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2)

whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). In this case, however, neither Sherr et al. nor Laes et al., alone or in combination, teaches or suggests the claimed invention.

Sherr et al. disclosed a method of inhibiting tumor cell proliferation using p19ARF. Sherr et al. did not demonstrate any protein fragment of p19ARF, let alone a specific protein fragment having the sequence of SEQ ID NO: 10, that is capable of inhibiting tumor cell proliferation. Additionally, none of the most frequently mutated residues in the Ink4A/ p19ARF region in cancers falls within the sequence of SEQ ID NO: 10 (for example, Gly-68, Pro-93, Arg-97, and Arg-114 are all outside amino acid residues 26-44). *See* Sherr et al. Col. 34, lines 56-62. Thus, Sherr et al. do not teach or suggest the importance of amino acid residues 26-44 in inhibiting tumor proliferation. Accordingly, it would not have been obvious to one skilled in the art the use of the p19ARF protein fragment having the sequence of SEQ ID NO: 10 for inhibiting proliferation of tumor cells.

The defect is not cured by Laes et al. Laes et al. do not teach or suggest which region is essential to the function of p19ARF. Laes et al. showed that in rodent hepatoma cells the p19ARF RNA is either absent or is expressed as a mutated form. In one mouse hepatoma cell line analyzed, the mutation would potentially encode a truncated p19ARF protein. The putative truncated p19ARF protein would retain only the N-terminal 15 amino acids of the wild type p19ARF. Laes et al. do not teach or suggest which portion of the large missing amino acid sequence (amino acid residues 16-169) is responsible for inhibiting tumor growth (Laes et al. Figure 2). Laes et al. do not teach or suggest the importance of amino acid residues 26-44 in inhibiting tumor growth. Moreover, Laes et al. do not teach or suggest whether a protein fragment of p19ARF, instead of the full length protein, can inhibit tumor cell proliferation. Thus, it would not have been obvious to one of skill in the art to use the p19ARF protein fragment having the sequence as set forth in SEQ ID NO: 10 to treat a tumor cell of epithelial cell origin. Thus, claim 1 as amended, and claims 9-10 would not have been obvious to one skilled in the art in view of the cited art. Consequently, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

VI. Conclusions

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

The Examiner in charge of this application is invited to contact the undersigned representative as indicated below if it is believed to be helpful.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

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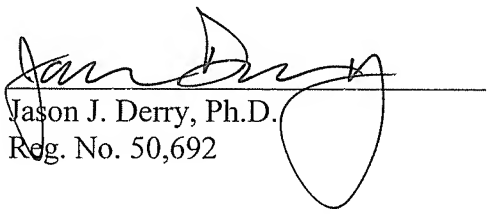
By: 
Jason J. Derry, Ph.D.
Reg. No. 50,692